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NON-ATHEROMATOUS AND UNCOMMON CAUSES OF MYOCARDIAL ISCHEMIA*

It is axiomatic that most individuals who suffer from myocardial ischemia do so by virtue of atherosclerotic changes in the coronary arteries. However, a small number of patients have myocardial ischemia from other causes. In these exceptional cases the myocardial ischemia often is an associated feature of another condition. It may be of only incidental pathologic interest or it may be the important element of the clinical features in a given patient. Appreciation of this fact may sometimes help to co-ordinate findings in individual patients which superficially seem to be of unrelated nature. It is to be emphasized that some of the conditions to be considered are very rare.

Non-atheromatous causes of myocardial ischemia may be classified as follows: (1) altered dynamics resulting from aortic valvular disease; (2) anatomic coronary ostial narrowing associated with diseases of the aortic valve or of the aorta; (3) coronary embolism; (4) manifestations of systemic disease and (5) congenital disease of the coronary arteries.

Altered Dynamics Associated With Aortic Valvular Disease

That altered dynamics associated with the various types of aortic stenosis, subaortic stenosis or aortic insufficiency may be responsible for myocardial ischemia is commonly recognized. Microscopic areas of myocardial necrosis may result from this type of functional interference with coronary circulation, but usually gross infarction of the myocardium is not found. Sudden death may occur, presumably on the basis of myocardial ischemia.

While syphilitic aortitis is the classic example of aortic insufficiency which may be responsible for coronary insufficiency, there are other varieties of incompetence of the aortic valve which may have the same effect. Among these are: (1) destructive changes caused by bacterial endocarditis and observed either during the bacteriologically active or the healed stages and (2) the lesion sometimes called "incomplete dissecting aneurysm". The latter lesion may appear spontaneously or as a result of trauma and is characterized by a break in the aortic wall, as in dissecting aneurysm, but without the extensive dissection by blood. The dilatation of the aorta seen in some patients with Marfan's syndrome (arachnodactyly)[1,2] may be hypothetically responsible for aortic insufficiency. In a rare case of congenital ventricular septal defect, changes in the adjacent leaflets of the aortic valve may cause dysfunction of the valve. The aortic valve itself is usually normal in cases in which an aneurysm of an aortic sinus (Valsalva) ruptures into the right ventricle or the right atrium. However, the run-off through the abnormal opening creates a functional disturbance similar to that of valvular insufficiency and may be a cause of coronary insufficiency.

Anatomic Coronary Ostial Narrowing Associated With Diseases of the Aortic Valve or of the Aorta

Coronary ostial narrowing associated with disease of the aortic valve or of the aorta is most commonly seen in syphilitic aortitis. Though medial scarring at the point where the coronary arteries exit from the aorta is often considered the cause of this change, it is probably the result of the intimal thickening of the aorta commonly associated with the medial disease characteristic of syphilitic aoritis.

Primary syphilitic involvement of the coronary arteries leading to the localized saccular aneurysm rarely occurs. When it does, coronary narrowing may result from a thrombus originating in the aneurysm and extending into the lumen of the parent vessel.

Coronary ostial narrowing by aortic intimal tissue, as in syphilitic aortitis, was observed in an instance of the unusual condition called "pulseless disease" or "primary arteritis of the aorta"[3]. In this state the aortic media, as well as the media of the branches of the aortic arch, is involved in acute or chronic inflammatory disease. Thrombosis, especially of the branches of the aortic arch, is a common phenomenon. Associated with the medial disease is a uniform inti-

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mal fibrous thickening of the thoracic aorta which leads to involvement of the coronary ostia.

Uncommonly, in cases of dissecting aneurysm of the aorta, there may be coronary narrowing when the dissecting hematoma extends proximally into the coronary branches. Even less frequent is the primary dissecting aneurysm of a coronary artery which may occlude the lumen of the involved vessel.

In a case of calcific aortic stenosis we observed a spur of calcified material so placed that the left coronary ostium was mechanically obstructed. In another case coronary ostial obstruction was observed after aortic valvulotomy for aortic stenosis in which, after the obstruction was relieved, the valvular tissue recoiled in such a way as to impinge on the left coronary ostium, causing extensive myocardial infarction.

Coronary Embolism

Whether coronary embolism occurs is debated by some, but from the nature of material sometimes observed in coronary arterial lumina there can be no doubt that coronary embolism must be recognized as an established phenomenon. In some instances the coronary embolus, though suspected, cannot be distinguished definitely from a locally occurring thrombus because of the co-existence of atheromatous coronary disease. Nevertheless, in some instances when the coronary arteries are normal, the distinction is easily made.

Coronary embolism may occur in chronic rheumatic mitral valvular disease. One may observe healed myocardial infarction in the absence of coronary atherosclerosis of significant degree in the patient with typical rheumatic mitral disease and left atrial thrombosis. In a case of mitral insufficiency in which acute myocardial infarction was associated, it was possible to uncover an embolus occluding the anterior descending coronary artery. Residual thrombi were present in the left auricular appendage.

In bacterial endocarditis coronary embolism is common, especially in the finer radicles of the coronary system. Emboli then account for the frequent association of microscopic-sized myocardial infarcts in patients with left-sided bacterial endocarditis. These infarcts are the most numerous of the various myocardial lesions in bacterial endocarditis, including those of suppurative and interstitial inflammatory nature. In a case of bacterial endocarditis we observed an infected vegetation plugging the anterior descending coronary artery with resultant gross myocardial infarction. At the site of such an embolus the artery becomes infected, and a complicating mycotic coronary aneurysm may develop. Usually, however, when there is occlusion of a large coronary artery, the patient succumbs before there is time for an aneurysm to form. Other rare types of coronary embolism include those of tumor tissue. We have seen this type of embolism in a case of the rare, pedunculated so-called myxoma of the left atrium[4]. At other times pulmonary neoplasms, whether primary or secondary, may be responsible for coronary embolism when the pulmonary veins are invaded. We observed such an example in a case of primary carcinoma of the lung in which many small coronary branches were occluded by tumor tissue.

On rare occasions we have seen paradoxical coronary emboli, either containing bland thrombotic material or neoplastic tissue. In cases of fat embolism the coronary radicles may be involved. Here the embolism is not necessarily paradoxical but may represent particles of fat which have passed through the pulmonary capillaries to the greater circulation.

Manifestations of Systemic Disease

Hypertension.—Quite apart from the frequent association of primary systemic hypertension with atherosclerosis of the coronary arteries, there may be non-atheromatous thickening of the media and intima of the small radicles of the coronary arteries. This process is shared by many organs in hypertension, including the kidneys. However, the changes in the small vessels rarely seem to be a cause of myocardial ischemia.

Rheumatic Fever.—Anatomic changes in the small coronary vessels of undetermined functional significance and similar to those in systemic hypertension are found in patients with healed rheumatic carditis[5]. These changes may be healed manifestations of acute arteritis, an uncommon lesion observed in the hearts of some patients dying from acute rheumatic carditis. I have detected a focus of acute myocardial infarction, involving the posterior papillary muscle of the left ventricle, in a child that had arteritis of the small coronary arteries as part of rheumatic pancarditis.

Periarteritis Nodosa.—The coronary system shares the changes of periarteritis nodosa with the arteries in other organs. These include acute arterial necrosis, the formation of aneurysms and thrombosis. Occlusion may lead to myocardial infarction as well as other manifestations of myocardial ischemia. Usually small areas of muscle are involved but gross infarction may result if a large vessel is occluded.

Thrombotic Thrombocytopenic Purpura.—The paradoxical condition in which thrombocytopenic purpura and a thrombotic tendency coexist is a systemic disorder. Included in its manifestations are lesions in the small intramural coronary arteries[6, 7]. Necrosis, aneurysm and thrombi are seen in these vessels and there may be associated small myocardial infarcts.

Anemia.—The anatomic manifestations in the coronary arteries in patients with anemia are marked by a tendency for development of intercoronary anastomoses[8]. These probably overcome local narrowings and thus tend to prevent certain portions of the myocardium from suffering from ischemia to a greater extent than other areas.

Metastatic Calcification.—Rarely calcification of the media of coronary arteries occurs in infants who have similar involvement in the ar-

teries of other organs, such as the kidneys, mesentery and adrenal glands. Parenchymal calcification also may exist. The intimal fibrous thickening associated with the medial calcification may cause significant narrowing and, in the case of the coronary arteries, may be associated with small areas of myocardial infarction. Several causes for this condition have been observed. Among these are diseases of bone, hyperparathyroidism, hypervitaminosis D, and chronic renal insufficiency[9, 10].

Congenital Diseases of the Coronary Arteries

Coronary Arteriovenous Fistula.—Under rare circumstances a congenital arteriovenous fistula may exist between the right coronary artery, on one hand, and on the other it might involve the coronary sinus, a tributary of it, the right atrium or the right ventricle[11-13]. The continuous murmur characteristic of such communications may lead the physician to suspect a patent ductus arteriosus or other functionally similar communications. Myocardial ischemia may be a consequence of the run-off of arterial blood through the fistula.

Anomalous Origin of a Coronary Artery from the Pulmonary Trunk.—Very rarely both coronary arteries have been described as arising from the pulmonary trunk. In such cases other serious cardiac defects were usually present, and life continued for only a few days after birth[14]. More commonly, one of the two coronary arteries arises anomalously while the other springs normally from the aorta[15, 16]. It is generally believed that such an anomalous origin of the right coronary artery is well tolerated. Though illustrative examples have been reported, others have been observed in which sudden death in relatively early life has appeared to be a manifestation of myocardial ischemia.

The situation with respect to anomalous origin of the left coronary artery is clearer. In about one third of the cases the patients fare like those who have an anomalous right coronary artery[17]. In the remaining two thirds a right-sided origin of the left coronary artery represents an early major problem, usually causing death before 1 year of age. That coronary insufficiency exists in these cases is attested by attacks thought to be those of angina pectoris, by electrocardiographic features of myocardial ischemia, and by evidence at necropsy of acute and healed myocardial infarction in the distribution of the left coronary artery. The ischemia is usually explained on the basis of flow of venous blood from the pulmonary trunk into the myocardium through the left coronary artery.

There is a different view of the pathogenesis of the ischemia. Recognizing that anastomoses normally exist between the right and left coronary arteries, it may be that from a functional point of view an arteriovenous fistula exists in the coronary system when the left coronary artery arises from the pulmonary trunk. If this is so, the tract begins at the right coronary artery, continues through anastomoses into the left coronary artery and terminates in the pulmonary trunk. This hypothesis suggests that rather than pulmonary arterial blood entering the myocardium, fully oxygenated blood from the right coronary artery is run off into the pulmonary artery. By virtue of the fistulous condition, the muscle in the distribution of the left coronary artery is ischemic.

Though this hypothesis has not been tested, so far as we are aware, it is of interest that symptoms usually are not present at birth, but their appearance is delayed until about 3 to 6 months after birth. It is then that the adult difference in pressure between the pulmonary and systemic arteries becomes established. At this stage the flow in the presumed fistulous tract would be more fully developed than earlier when there is less difference between the arterial pressures in the two circulations.

Further support of this hypothesis comes from the fact that in some instances in which the left coronary artery arises anomalously, the right coronary artery is grossly tortuous and dilated. Such a phenomenon is frequently observed in other portions of the body in arteries proximal to arteriovenous fistulas.

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The opinions and conclusions expressed herein are those of the author and do not necessarily represent the official views of the Scientific Council of the American Heart Association.

ABSTRACTS OF PAPERS
for
THE 29th ANNUAL SCIENTIFIC SESSIONS,
AMERICAN HEART ASSOCIATION

The 29th Annual Scientific Sessions of the American Heart Association will be held in Cincinnati, Ohio, October 27, 28, 29, 1956 in conjunction with the Association's Annual Meeting. The deadline for submission of abstracts has been extended to June 15. Abstracts will be accepted only on forms which may be obtained from the Medical Director, American Heart Association, 44 East 23rd Street, New York 10, New York.

Papers intended for presentation should be based on original investigations in or related to the cardiovascular field. The abstracts must be 300 words or less and should contain in summary form the results obtained and the conclusions reached. Abstracts must be submitted in triplicate.

The Scientific Sessions this year will feature an enlarged section for Scientific Exhibits. Requests for space and application forms can also be obtained from the Association's Medical Director. The deadline for these applications has been extended to June 15, 1956. All exhibit applications will be acted upon by the Program Committee of the Scientific Council.

AMERICAN HEART ASSOCIATION TO REVIEW U.S. PAPERS FOR INTER-AMERICAN CONGRESS

A committee of the American Heart Association will review all abstracts of papers by United States physicians and research scientists who wish to make presentations at the Inter-American Congress of Cardiology in Havana, November 11-17. The congress is sponsored by the Inter-American Cardiologic Society and their regulations provide that papers must be submitted through the national cardiologic society of the country in which the author resides.

Abstracts (200 words or less) must be submitted in duplicate to the Medical Director, American Heart Association, 44 East 23rd Street, New York 10, before July 1, 1956.